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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,446	07/29/2003	Navin Vaya	1296-015	7784

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EXAMINER	
MERCIER, MELISSA S	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/630,446	VAYA ET AL.	
	Examiner	Art Unit	
	MELISSA S. MERCIER	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-33 and 36-74* is/are pending in the application.

4a) Of the above claim(s) *30,31,73 and 74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-29, 33, 36-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 29, 2007 has been entered.

Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application. Claims 1, 4-33, and 36-74 remain pending in this application. Claims 30-31 and 73-74 remain withdrawn as reading on non-elected groupings. Therefore, claims 1, 4-29, 33, 36-72 remain under prosecution in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-29, 33, 36-72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has amended the claims to employ consisting essentially of and consisting of terminology, however, after a review of the specification, the examiner has not been able to locate support for such a limitation. The specification uses comprising language as to the content of the dosage form and lists numerous excipients for inclusion. In the arguments submitted by Applicant on November 29, 2007, it is disclosed that the claim terminology was changed to exclude the presence of talc. Applicant has not provided adequate written description of the change in terminology. Applicant has not provided a location within the lengthy specification as to where support can be found. The examiner notes that the specification discloses the inclusion of various excipients within the dosage form. Applicant has not disclosed what are considered essential components to the dosage for and what is expressly excluded from the dosage form. Applicant is requested and welcomes to disclose the location of such support within the specification if applicant believes such support does exist. The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. *In re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) For the purposes of searching for and applying prior art under 35 USC 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."

See, e.g., *PPG*, 156 F.3d at 1355, 48 USPQ2d at 1355. **This is a new matter rejection.**

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-5, 8-11,14-29, 32-33, 36-37, 40-60, 62-65, 68-69, and 71-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and Webb et al. (US Patent 4,996 061).

Glassman teaches, "a super-fast-starting, slow release medicinal tablet, wherein the tablet is comprised of two layers of compressed matrix that are fused together by means of a readily dissolvable adhesive substance, and in which one of the layers is a lightly compressed top layer containing a pure unadulterated, uncoated, active drug and which has one or more radial grooves in it's top surface to enhance rapid breakdown of the tablet; and the other layer has a strongly compressed portion comprised of a medically inert or inactive matrix having embedded throughout a multitude of pellets, each containing an active ingredient and having enteric coatings of various thicknesses so as to variably

delay disintegration of the pellets" (abstract).

Glassman does not teach the pharmaceutical active as being highly soluble, the immediate release portion being a low dose, or the modified release being a high dose.

Paradissis teaches, "formulations composed of a mixture of 0 to 50% of an immediate release particle containing a core of drug, inert spherical substrate particles and binder, coated with talc and up to 100% of an extended release particle comprising the immediate release particle coated with a dissolution modifying system containing plasticizers and a film forming agent, wherein the particle size of the extended release formulation is -10+60 mesh" (column 3, lines 21-33). The Examiner is interpreting the particle stated particle size for the extended release particles to include the coating; therefore the coating would be a micro matrix.

While the Paradissis patent does not specifically teach that the pharmaceutical actives must be highly soluble, it does teach, "a wide variety of medicaments which are orally administered as tablets maybe used, these include acetaminophen, which applicant provides as one example of a highly soluble active. "The drugs used in the formulations of Paradissis may be selected from a wide variety of pharmaceutical formulations with particular pharmaceutical compounds being analgesics, anti-inflammatories, antihistamines, antitussives, expectorants, decongestants, narcotics, antibiotics, bronchodilators, cardiovasculars, central nervous system (CNS) drugs, metal salts, minerals, vitamins and mixtures thereof" (column 3, lines 34-41). Further it would be obvious to one of ordinary skill in the art to substitute any active pharmaceutical into the teachings of Glassman and Paradissis.

Paradissis further teaches, "water-insoluble hydrophobic agents, such as diethyl phthalate, diethyl sebacate and castor oil are used to delay the release of water-soluble drugs, such as potassium chloride" (column 6, lines48-52) and "the film forming agents, which are also preferably employed in a spraying solution along with the plasticizer, may be selected from a wide variety of film forming materials. Preferable materials, however, may be selected from the group consisting of acrylic and methacrylic acid copolymers and cellulose derivatives. Exemplary cellulose derivatives include ethylcellulose, methylcellulose, cellulose acetate, hydroxypropylcellulose, hydroxypropylmethylcellulose, hydroxyethylcellulose and mixtures thereof" (column 7, lines 4-13).

Additionally, Paradissis teaches, "the extended release particles of the invention are then prepared by taking the immediate release particles and coating them with a dissolution modifying system which functions as a diffusion membrane around the coated core. The dissolution modifying system contains a plasticizer and a film forming agent which is applied by spraying the immediate release particles with about 2 to about 35% by weight of the dissolution modifying system coating. The dissolution modifying system is designed to encapsulate the particles and modify the drugs dissolution profile so that a sustained/extended drug release rate is obtained. In other words, the system is formulated to each drug profile to permit a release of the drug from the particles over a 12 to at least 24 hour period (column 6, lines 32-45).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the percentages of coating on the micro matrix particles in order to provide the release of the modified release component that was desired.

Paradissis additionally teaches, "preferred plasticizers may be selected from the group consisting of diethyl phthalate, diethyl sebacate, triethyl citrate, crotonic acid, propylene glycol, butyl phthalate, dibutyl sebacate, castor oil and mixtures thereof" (column 6, lines 46-50).

Paradissis teaches, "formulations composed of a mixture of 0 to 50% of an immediate release particle containing a core of drug, inert spherical substrate particles and binder, coated with talc and up to 100% of an extended release particle comprising the immediate release particle" (column 3, lines 21-29).

While Paradissis does not teach the exact ratios of immediate release to modified release, it would be obvious to one of ordinary skill in this art to expand upon Paradissis to arrive at the instant claims.

Paradissis further teaches as a preferred embodiment "the formulation comprises from 0 to 50% of an immediate release particle containing a core of at least one drug, and up to 100% of an extended release particle which comprises the immediate release particle, additionally coated with a dissolution modifying system and optionally additional drug (column 3, lines 66-69, column 4, lines 1-4).

It would have been obvious to one of ordinary skill in the art that the time the invention was made to combine additional active ingredients to the tablet in order "to

reduce the minimum daily number of doses from which the drug is uniformly released over a desired extended period of time" (column 1, lines 30-33).

Additionally, Paradissis teaches, "the rate of release of the pharmaceutical formulation may be described according to standardized dissolution testing procedures as found in the U.S. Pharmacopoeia XXII, where less than 50% of the drug is released within 1 hour of measurement and not less than 70% of the drug is released at the targeted dosing period, such as a 12 to at least 24-hour period (column 6, lines 39-45). It is the Examiners position that Paradissis target dosing period includes the 6-hour dosing period of the instant application.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the coating thicknesses and particle sizes in order to make a dosage unit which will meet the release profile sought. One of ordinary skill in this art would be able to modify release profiles without undue experimentation.

Regarding Claim 28, Glassman teaches his "super-fast-acting, slow release tablet is capable of rapidly and predictably entering the Therapeutic Zone. The herein disclosed super-fast-acting, slow-release tablet (S/R) predictably enters into the Therapeutic Zone in the shortest possible time (less than one hour). That is 4-5 times faster than any known sustained release tablet, and it offers immediate and lasting therapeutic relief covering a period of 12 or more hours (column 4, lines 48-57). The Examiner is interpreting the 12 hours or more to be twice a day dosing.

Regarding Claim 29, Glassman teaches a study on asthmatic children who where given single dosages of uncoated tablets of Theophylline, which was not

absorbed fast enough and therefore invented his tablet which combined uncoated and coated tablets. (column 4, lines 58-68). Therefore, it would be obvious to assume that Glassman intends his dosage forms to be used by human beings.

It is generally considered to be prime facie obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose in order to form a composition that is to be used for an identical purpose. The motivation for combining them flows from their having been used individually in the prior art, and from them being recognized in the prior art as useful for the same purpose. As shown by the recited teachings, instant claims are no more than the combination of conventional components of coating materials used in pharmaceutical compositions. It therefore follows that the instant claims define prime facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Glassman with the teachings of Paradissis in order to provide "the advantage of administering in a minimum of daily doses from which a drug is uniformly released over a desired, extended period of time. Various techniques have been developed for the purpose of including a pharmaceutical preparation comprising a drug-containing particle with a coating layer and a pharmaceutical preparation comprising a continuous matrix with a drug dispersed therein, such as embedded into a rigid lattice of resinous material" (Paradissis, column 1, lines 28-35).

Glassman and Paradissis do not teach a tablet, in which the inner portion is covered by the outer portion from all sides except the top surface that remains uncovered.

Webb teaches "a variation of the compression-coated tablet is the inlay tablet, also referred to as a dot, or bull's-eye tablet. Instead of an inner core zone being completely surrounded by an outer coat, one surface of the zone corresponding to an inner core zone is exposed. These tablets have at least two discrete zones of granulation compressed together, i.e., an inlay zone and a base zone. The preparation of inlay tablets is similar to the preparation of compression-coated tablets except that a surface of coating is eliminated" (column 6, lines 3-15).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Glassman and Paradissis with the tablet of Webb in order to provide sustained-release of an active pharmaceutical with immediate release of another or the same active pharmaceutical.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. Applicant argues the change in claim terminology from comprising to consisting essentially of required the exclusion of talc from the instant claims. The examiner disagrees. The prior art teaches and Applicant acknowledged the talc is used as a sort of glue to hold the layers of the tablet together. The talc does not materially affect the properties of the tablet including the release profiles or alter the characteristics of the

active agents. The teachings of Glassman regarding the optional inclusion of additional components also do not effect the material properties of the composition, since they are not required by the teachings. They may or may not be added depending on the desired function and dissolution properties of the dosage form.

Applicants have further argues Paradises additionally discloses particles containing a core of drug, inert spherical substrate particles and binders coated with talc, which is employed to prevent the drug layer from interfering with film formation on the particles and to prevent drug migration during storage. The examiner disagrees with applicants assertion that the talc must be excluded based on their newly presented claim language. The examiner points applicant to the new matter rejection above which includes an explanation of the transitional phrases ability to exclude certain components. It is further noted that Applicant specification on page 14, lines 10-17, allows for the inclusion of diluents, binders, lubricants, including talc, surfactants, disintegrant, plasticizers, anti-tack agents, opacifying agents, pigments and such, and acknowledged the exact choice of the excipients and their amounts will depend to some extent on the final oral dosage form.

Regarding Applicants arguments' regarding the Webb reference, Applicant appears to be arguing the components of used in the Webb dosage form. The examiner concedes the dosage form components of Webb are different from the instant claims. Webb was relied on to demonstrate the type of tablet, i.e. a bulls eye tablet is known in the art and it would have been obvious to a person of ordinary skill to have incorporated that particular tablet design in order to provide sustained-release of

an active pharmaceutical with immediate release of another or the same active pharmaceutical.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Claims 6-7,12-13, 36-39, and 44-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glassman (US Patent 4,503,031) in view of Paradissis et al. (US Patent 5,445,829) and Webb et al. (US Patent 4,996 061) and further in view of Lerner et al. (US Patent 5,840,332).

The teachings of Glassman, Paradissis and Webb as they apply to claim 1 are described above and applied in the same manner.

Glassman, Paradissis and Webb do not teach the specific hydrophobic release controlling agents of the instant claims.

Lerner teaches, "a gastrointestinal delivery system is provided. The system comprises a drug in combination with a core material, the core being surrounded by a water-insoluble or relatively water-insoluble coating material in which particulate water-insoluble material is embedded. When the delivery device enters the gastrointestinal tract, the particulate matter takes up liquid, thus

forming channels interconnecting the drug-containing core with the outside of the delivery device. These channels allow the release of drug from the core into the gastrointestinal tract. By controlling parameters in the device, such as the core material, carrier material in the coating, and particulate matter, the location of release of the drug can be carefully controlled" (abstract).

Additionally, Lerner teaches, "the coating includes, but is not limited to, any combination of a water-insoluble polysaccharide, water-insoluble crosslinked polysaccharide, a water-insoluble polysaccharide metal salt, a water-insoluble crosslinked protein or peptide, a water-insoluble crosslinked hydrophilic polymer in a dried powder form as the particulate and any hydrophobic polymer coating known in the art as the water-insoluble carrier. Specific examples of the water-insoluble carrier include, but are not limited to, Eudragit E.TM., Eudragit NE.TM., Eudragit RL.TM., Eudragit RS.TM., ethylcellulose, shellac, zein, and waxes" (column 9, lines 38-65).

It is generally considered to be prime facie obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose in order to form a composition that is to be used for an identical purpose. The motivation for combining them flows from their having been used individually in the prior art, and from them being recognized in the prior art as useful for the same purpose. As shown by the recited teachings, instant claims are no more than the combination of conventional components of coating materials used in pharmaceutical compositions. It therefore follows that the

instant claims define prime facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. Applicant's arguments regarding Glassman, Paradises, and Webb are discussed above. Applicant further argues Lerner's composition is directed to a composition comprising a core and coating wherein the core contains drug with carrier material and the functional properties of the formulated dosage unit. While the examiner concedes the dosage form is different and may perform different functionally from the claimed invention, the reference is relied on to show specific hydrophobic polymer coatings routinely used as rate controlling agents since the Paradissis reference discloses a generic teaching of hydrophobic polymers. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

No claim is allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA S. MERCIER whose telephone number is (571)272-9039. The examiner can normally be reached on 7:30am-4pm Mon through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Melissa S Mercier/
Examiner, Art Unit 1615

/Michael P Woodward/
Supervisory Patent Examiner, Art Unit 1615